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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,843	09/17/2001	Sheena M. Loosmore		5498

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,843	LOOSMORE ET AL.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,25 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. The preliminary amendment filed September 27, 2002 has been entered. The examiner acknowledges amendments to the specification. Claims 6-24 and 26 have been cancelled. Claim 27 has been newly added. Claims 1-5, 25 and 27 are under consideration in this office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn in view of applicants' amendments:

a) the rejection of claims 6-24 and 26 under 35 U.S.C. 112, first paragraph;

b) the rejection of claim 26 under 35 U.S.C. 112, second paragraph;

c) the rejection of claim 26 under 35 U.S.C. 101;

d) the rejection of claims 6-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barenkamp et al., (WO 97/36,914) in view of Loosmore et al. (US Patent 5,506,139);

e) the rejection of claim 23 under 35 U.S.C. 103(a) as being unpatentable over Barenkamp et al., (WO 97/36,914) and Loosmore et al. (US Patent 5,506,139) in view of Anilionis et al. (US Patent 5,098,997);

f) the provisional rejection of claims 6-24 under 35 U.S.C. 101; and

g) the provisional rejection of claims 1-5 and 25-26.

Response to Arguments

3. Applicant's arguments filed September 27, 2002 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. The rejection of claims 1-5 and 25 under 35 U.S.C. 112, first paragraph is maintained for reasons already of record. The rejection was on the grounds that the specification would be enabled for an immunogenic composition comprising the analog H91A Hin47 having decreased protease activity and a recombinant high molecular weight (rHMW) protein to confer protection against *Haemophilus influenzae*, but did not reasonably provide enablement for an immunogenic composition comprising at least two different antigens of *Haemophilus influenzae* where at least one is an adhesin and the other is not an adhesin.

Applicants assert that the enablement should not be limited to recombinantly produced HMW protein and should not be limited to H91A Hin47 analog, but should extend to at least any non-proteolytic analog of the Hin47.

In response to applicant's argument that the claims should not be narrowly construed, it is noted that the features upon which applicant relies are not limited to at

least any non-proteolytic analog of Hin47. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant has supplied no correlation data to an immunogenic composition with at least two different antigens wherein one is an adhesin and the other is not, wherein the composition will confer protection in a host against diseases caused by *H.influenzae*. It is noted that applicants' specification appears to make the conclusion that any immunogenic composition, comprising at least two different antigens of *Haemophilus influenzae* wherein at least one is an adhesin and the other is not an adhesin is capable of conferring protection in a host against disease caused by *Haemophilus influenzae,* can be used without any substantiating evidence. Moreover, applicants' examples only teach the use of recombinantly produced HMW proteins.

Thus applicants statement that a skilled artisan can determine whether a protein is an adhesin, is not persuasive, since in this case a skilled artisan has to do more than determine adhesins. The claims are drawn to an immunogenic composition which confers protection in a host against *H.influenzae* diseases, thus a skilled artisan would have to de novo create an immunogenic composition against *H. influenzae* that confers protection. Since applicants have not provided guidance as to the nature and extent of the changes that must be made to enable one of ordinary skill in the art to make, without undue experimentation, an immunogenic composition comprising at least two different antigens of *Haemophilus influenzae* wherein at least one is an adhesin and the other is not an adhesin, this experimentation would be undue. Given the lack of

guidance contained in the specification and the unpredictability for making an immunogenic composition comprising at least two different antigens of *Haemophilus influenzae* wherein at least one is an adhesin and the other is not an adhesin, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Applicants point to the specification wherein one skilled in the art would be advised that a non-adhesin protein is a non-proteolytic analog of Hin47 protein or other non-proteolytic heat shock proteins, however the limitations from the specification are not read into the claims. The instant claims are significantly broader than the recitations in the specification.

However, it is the examiner's position that the specification fails to provide an enabling disclosure for the use of any immunogenic composition comprising, at least two different antigens of *Haemophilus influenzae* wherein at least one is an adhesin and the other is not an adhesin, that meets the limitations recited in the claims. Applicants' have provided no guidance to enable one of ordinary skill in the art as to how to determine, without undue experimentation, other immunogenic compositions. There is no requirement for the use of only the incorporation a H91A Hin47 analog having decreased protease activity and a recombinant HMW protein to confer protection against *Haemophilus influenzae.* Therefore, the rejection is maintained despite applicants' arguments given the lack of guidance contained in the specification and the unpredictability for determining an acceptable immunogenic composition, that one

skilled in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The rejection of claims 1-5, 25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Barenkamp et al., (WO 97/36,914) in view of Loosmore et al. (US Patent 5,506,139) is maintained for reasons already of record.

The rejection was on the grounds that it would have been prima facie obvious at the time of applicant's invention to modify an immunogenic composition to confer protection against *Haemophilus influenzae* comprising at least two different antigens, wherein one is a heat shock protein as taught by Loosmore et al., and the other is a high molecular weight adhesin protein, HMW1 or HMW2 which are important protective antigens as taught by Barenkamp et al., (WO 97/36,914), because Loosmore et al., teach that analogs of Hin47 with reduced protease activity from *Haemophilus influenzae* are useful in vaccination against diseases caused by *H. influenzae* or other bacterial pathogens and these proteins are capable of eliciting protective opsonizing or bactericidal antibodies.

Applicant's urge that there is no suggestion to combine the references since the references state that other immunogenic or immunostimulating materials can be within the composition and therefore lack a specific teaching to combine the mutant Hin47 protein with the High Molecular Weight (HMW) protein in an immunogenic composition. This argument is not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, it would have been obvious at the time of applicant's invention to have an immunogenic composition to confer protection against *Haemophilus influenzae* comprising at least two different antigens, where one is a well known high molecular weight adhesin protein, HMW1 or HMW2, which are important protective antigens that should comprise one component of a multi-component non-typeable *H. influenzae* vaccine as taught by Barenkamp et al., (WO 97/36,914), in combination with the analog of Hin47 which is a non-proteolytic heat shock protein with substantially reduced proteolytic activity useable in other immunogenic preparations as taught by Loosmore et al.

Furthermore, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also, In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). See In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987) ("Based upon the prior art and the fact that each of the three components of the composition used in the claimed method is conventionally employed in the art for treating cooling water).

In this case, no more than routine skill was required at the time of applicants invention to combine two well known antigens of *H.* influenzae, an adhesin and a heat shock protein, since the prior art shows that both: elicit an immunogenic response in a host; provide protection against a *H. influenzae* infection; and are useful in immunogenic compositions in combination with other immunostimulating antigens. Accordingly, both antigens are useful for the same purpose, to form an immunogenic

composition to be used for that very same purpose. Thus, applicant's argument is unpersuasive.

Applicant argues that there is no motivation provided from the disclosures to combine different proteins derived from the same pathogen and there is no motivation to select Hin47 however this argument is not persuasive.

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). The synergy concept is a well established in the art and it would require no more then routine skill to utilize two well-known components that have similar purpose and are capable of achieving similar results in a single composition as instantly claimed. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time of appellant's invention to have an immunogenic composition to confer protection against *Haemophilus influenzae* comprising at least two different antigens, wherein one is a heat shock protein as taught by Loosmore et al., and the other is a high molecular weight adhesin protein, HMW1 or HMW2 which is an important protective antigen as taught by Barenkamp et al., (WO 97/36,914), because Loosmore et al., teach that analogs of Hin47 elicit an immune response capable of producing anti-Hin47, opsonizing or bactericidal antibodies, and provides data that show Hin47 analogs provide protective ability.

As previously stated, it would have been obvious at the time of applicant's invention to have an immunogenic composition to confer protection against *Haemophilus influenzae* comprising at least two different antigens, where one is a high molecular weight adhesin protein, HMW1 or HMW2 and the other component is an analog of Hin47. Thus applicant's argument is not persuasive.

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is

703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communication.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
December 10, 2002

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600